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10/591,521	09/01/2006	Hiroharu Kawahara	125192.00501	1684

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EXAMINER	
KIM, ALEXANDER D	
ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,521	KAWAHARA, HIROHARU	
	Examiner	Art Unit	
	ALEXANDER D. KIM	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,20 and 21* is/are pending in the application.

4a) Of the above claim(s) *8-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,20 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/01/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. By virtue of a preliminary amendment filed on 12/20/2007, claim 19 has been canceled. Thus, claims 1-18 and 20-21are pending in this instant case.

Election

2. Applicant's election of Group I, Claims 1-7 and 20-21, is acknowledged. Because applicant did not distinctly and specifically point out the status of traverse in the restriction requirement, the election has been treated as an election without traverse (M.P.E.P. § 818.03(a)).

Claims 8-18 are withdrawn from consideration as non-elected inventions. Claims 1-7 and 20-21 will be examined herein.

Priority

3. The instant application is a 371 filing of the International Application No. PCT/JP04/16276 filed on 10/27/2004. The Examiner notes that the requirements of national stage entry of the instant application had been completed (note assigned U.S. filing date) within 30 months of the earliest claimed priority date; the related international application includes both a search report and a preliminary examination report.

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) to a foreign patent application JP2004-056551 (Japan, filed on 03/01/2004) filed without English translation.

Information Disclosure Statement

3. The information disclosure statement (IDS) filed on 09/01/2006 has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy.

Claim Objections

4. Claims 1-7 and 20-21 are objected to because of the following informalities:

(a) Claim 1 (Claims 2-6 and 20-21 dependent therefrom) recites "0.1 to mg per 1,000,000 cells". It should be ---"0.1 to 1.0 mg per 1,000,000 cells---. .

(b) Claim 7 recites 10 .mu.g/day. It should be ---10 ug/day---.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 20-21 are rejected under 35 U.S.C. 112, first paragraph, enabling deposit, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one

skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to employ novel biological material, specifically the host cell strain named as SC-02MFP (Accession Number FERM BP-10087) and SC-01MFP (Accession Number FERM BP-10077). Since the biological material are essential to such an invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. If the biological materials are not so obtainable or available, the requirements of 35 USC 112 §1st may be satisfied by a deposit of the biological materials.

This Office action reminds applicants that an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific of record over his or her signature and registration number, stating that the specific biological materials will be irrevocable and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein.

Applicant's attentions is directed to MPEP section 2400 in general, and specifically to 2411.05, as well as to 37 CFR 1.809(d), wherein it is et forth that "the specification shall contain the accession number for the deposit, the date of the deposit, "the name and address of the depository, and a description of the deposited material sufficient to specifically identify it and to permit examination". The specification should be amended to include this information, however, applicant is cautioned to avoid entry of new matter into the specification by adding any other information.

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6. Claims 1-7 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to a human cell strain enabling the continuous production of a desired protein with high efficiency (or enabling the continuous production of a desired protein at a yield of 1 ng-10 ug/day per 1,000,000 cells at least over a 2 month period for claim 7), comprising: a human cell strain established by transforming a human cell strain whose total intracellular protein weight is 0.1 to 1.0 mg per 1000000 cells; with said human cell strain being further characterized in that after a gene encoding a desired protein is transfected into it, the transfected cell is subsequently cultured. Claims 2-6 are a human cell strain of Claim 1 with additional limitation as recited in the claims.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants

must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these (paraphrased from *Enzo Biochemical Inc. v. Gen-Probe Inc.* (CAFC (2002) 63 USPQ2d 1609).

The instant specification teach human cell strains SC-02MFP (Accession Number FERM BP-10078) or SC-01MFP (Accession Number FERM BP-10077). However, the breadth of claim includes any human cell strain (including but not limited to any mutant thereof) enabling the continuous production of any protein with high efficiency over any given time period after transforming with any gene encoding any protein. The prior art by Kawahara et al. (1999, Human Antibodies, Volume 9, pages 83-87) teaches one species of human cell strain encompassed within a claimed genus human cell. The specification discloses two species of claimed human cell strain (i.e., SC-02MFP and SC-01MFP) which can be used for a production of protein. However, the prior art and the instant specification do not describe any human cell strain that can be used for protein production sufficiently to represent the correlation between the structure of any human cell strain and function of continuously producing any desired protein. Thus, the instant specification and the prior art cannot describe the structure of a very broad claimed genus human cell line enabling the continuous production of a

desired protein; and one skilled in the art would not be in possession of the claimed genus by the instant specification.

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7. Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for SC-02MFP (Accession Number FERM BP-10078) or SC-01MFP (Accession Number FERM BP-10077), if said cells meet the biological materials deposit requirement (as stated above), does not reasonably provide enablement for any human cell strain enabling (or capable) of continuously producing a desired protein.

The specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use of the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in

determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The nature of the invention is drawn to human cell strains SC-02MFP (Accession Number FERM BP-10078) or SC-01MFP (Accession Number FERM BP-10077). However, the breadth of claim includes any human cell strain (including but not limited to any mutant thereof) enabling the continuous production of any protein with high efficiency over any given time period after transforming with any gene encoding any protein. The prior art by Kawahara et al. (1999, Human Antibodies, Volume 9, pages 83-87) teaches one species of human cell strain encompassed within a claimed genus human cell. The applicant teaches two species of claimed human cell strain (i.e., SC-02MFP and SC-01MFP) which can be used for a continuous production of protein. However, applicants disclose no direction or guidance on how to make and use any other human cell strain enabling the continuous production of any desired protein. Thus, the specification and prior art fail to describe how to make and use the claimed genus human cell strain sufficiently. Therefore, it is unpredictable for any human cell strain to be used in the continuous production of any desired protein. Thus, it is unpredictable for any human cell encompassed by the claims for one skilled in the art to make and use the full scope of claims. The said unpredictability makes the relative skill

required in the art very high. For all of the above reason, it would require undue experimentation necessary for any human cell strain.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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8. Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Kawahara et al. (1999, Human Antibodies, Volume 9, pages 83-87).

Claim 1 is drawn to a human cell strain enabling the continuous production of a desired protein with high efficiency (or enabling the continuous production of a desired protein at a yield of 1 ng-10 ug/day per 1,000,000 cells at least over a 2 month period for claim 7), comprising: a human cell strain established by transforming a human cell strain whose total intracellular protein weight is 0.1 to 1.0 mg per 1,000,000 cells; with said human cell strain being further characterized in that after a gene encoding a desired protein is transfected into it, the transfected cell is subsequently cultured. Claims 2-6 are a human cell strain of Claim 1 with additional limitation as recited in the claims.

Kawahara et al. teach a human parent cell line from T lymphoma named as ICLU-T, which were "recloned in ITES-ERDF medium by limiting dilution" (see middle of

left column, on page 84). It is noted that the Claims 1-7 are product by process, which "ARE NOT LIMITED TO THE MANIPULATIONS OF THE RECITED STEPS, ONLY THE STRUCTURE IMPLIED BY THE STEPS" (see MPEP 2113 [R-1]). The recitation of "established by transforming a human cell strain whose total intracellular protein weight is 0.1 to 1 mg per 1,000,000 cells" in claim 1 is a process steps which does not result in any structural limitation of claimed human cell strain. The recitation of "further characterized in that after a gene encoding a desired protein is transfected into it, the transfected cell is subsequently cultured" is not structural limitation of claimed human cell strain in the Claim 1, because said characterization would be acquired "after a gene encoding a desired protein is transfected" (emphasis added), that is only if the gene is transfected, which only implies the claimed human cell strain is enabled (or capable) of producing a protein. Kawahara et al. teach that "ICLU-T expressed CD2, CD4, CD8 and CD19, as shown in Fig. 2" (see middle of left column, on page 87); thus, the ICLU-T cell has (or "is enabling") ability for protein expression with high efficiency when the cell is transfected with a gene appropriate for expression and when subsequently cultured. Thus, ICLU-T cell meets the limitation of claim 1 because the ICLU-T cell would produce a protein with high efficiency if the cell were transfected with a vector with a gene appropriate for expression, wherein high efficiency is a broad terminology which can be met by any transfected expression system. Also, the instant specification discloses "human leukemia T-cell strain PEER" (e.g., ICLU-T, which was separated from human T cell acute lymphocytic leukemia, PEER, see Abstract of Kawahara et al.) can be used to "allows a long term stable protein production" (see page 6, lines 19-20).

Thus, the ICLU-T meets the limitation of Claim 1. The ICLU-T cell of Kawahara et al. meets the limitations of Claims 2-3, because Claims 2-3 are drawn to the human cell strain of claim 1 that is derived from RPMI8226 or KMS-12BM cells (emphasis added) and Claims 2-3 are not limited to the cells of PRMI8226 or KMS-12BM. Because claimed cells in Claims 2-3 are derivatives of PRMI8226 or KMS-12BM, the claimed human cell strain do not require to have any structural features of RPMI8226 or KMS-12BM cells.

Claims 4-5 recite the step of "choosing --- ; and mutating said cell clones with carcinogens" which is a product by process type limitation, which "ARE NOT LIMITED TO THE MANIPULATIONS OF THE RECITED STEPS, ONLY THE STRUCTURE IMPLIED BY THE STEPS" (see MPEP 2113 [R-1]). The only structure implied by the step in Claims 4-5 are "a doubling time of 18 to 24 hours and a 90% rate of cloning by limited dilution method". Figure 3 on page 86 by Kawahara et al. disclose the doubling time is within 18 to 24 hours at a certain time (see the steepest line by filled triangle during 3rd and 4th day of growth). Since the ICLU-T is the cell cloned by the limiting dilution as described above, the selected ICLU-T by Kawahara et al. has 100% rate of cloning. Thus, the ICLU-T of Kawahara et al. meets the limitations of Claims 4 and 5. The ICLU-T cell "can continuously produce the desired protein", if the cell is transfected, in the ERDF medium since the cell of Kawahara et al. grew in ITES-ERDF serum free medium consisted of ERDF medium" (see left column, line 9, on page 84) for three weeks (see left column, middle, on page 84). ; thus, meeting the limitation of Claim 6. Claim 7 recites "enabling the continuous production of a desired protein at a yield of 1

ng-10 ug/day per 1,000,000 cells at least over a 2-month period" is a preamble. According to MPEP 2111.02 [R-3], "statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim." In this case, the recited term in preamble merely reciting the intended use and does not results in a structural difference in the claimed human cell strain. Thus, the ICLU-T cell by Kawahara et al. meets the limitations of Claims 1-7.

Conclusion

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9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEXANDER D. KIM whose telephone number is (571)272-5266. The examiner can normally be reached on 11AM-7:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Alexander D Kim/
Examiner, Art Unit 1656

/Richard G Hutson, Ph.D./
Primary Examiner, Art Unit 1652